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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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PHILIP S. JOHNSON
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

EXAMINER	
NOLAN, JASON MICHAEL	

ART UNIT	PAPER NUMBER
1626	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/695,347	LI ET AL.	
	Examiner	Art Unit	
	JASON NOLAN	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 January 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,17-23 and 32-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,17-23,32,34,36 and 37* is/are rejected.

7)☐ Claim(s) *33 and 35* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after allowance or after an Office action under *Ex Parte Quayle*, 25 USPQ 74, 453 O.G. 213 (Comm'r Pat. 1935). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 01/28/2009 has been entered.

This application has been transferred to Jason M. Nolan from Abigail Fisher. In the previous Office Action, mailed 10/28/2008, Examiner Fisher rejected Claims 1-3, 6-8, 17-19, 22, 23, & 28 under 35 USC 103 over Choi *et al.* (WO 9920745) in view of Chen *et al.* (US 5,922,352) and Sangekar *et al.* (US 4,992,277). As filed, Claims 1-8, 17-23, & 32-37 are pending in the instant application; of which, Claims 1 & 17 are currently amended and Claims 32-37 are new.

Response to Amendment and Arguments

Applicant's amendments with respect to Claims 1, 17, & 32-37 have been fully considered and are entered. Applicant's arguments filed 01/28/2009 have been fully considered but they are not persuasive. Applicants argue that the teachings of Kim *et al.* (WO 99/20745; formerly referred to by the Agent "Choi" and not the inventor Kim *et al.*); Chen *et al.* (US 5,922,352); and Sangekar *et al.* (US 4,992,277) taken alone or in any combination, fail to render the instant claims obvious.

Specifically, Applicants argue that Kim *et al.* fails to teach the specific overcoating composition of the instant invention; that there is no teaching or suggestion of delayed release properties; that the instant overcoating composition is more than predictable use; that the instant overcoating composition is made by a different technique; and that the granules in Kim *et al.* are not a compressed core.

Applicants argue that Chen *et al.* does not teach or suggest the specific overcoating composition; that there is no teaching of delayed release properties; and that there is no teaching of compressed granules.

Further, Applicants argue that Sangekar *et al.* is distinguished from the instant application because the patent is drawn to an immediate release drug formulation.

The Examiner is not persuaded by Applicant's arguments for the following reasons. First, Applicant incorrectly attempts to restrict the scope of what the prior art teaches by what is exemplified and by what the differences are between those exemplified compositions and the instant compositions. For instance, Applicant admits that Kim *et al.* teaches that hydroxypropylmethylcellulose, carrageenan and gellan gum are useful as coating materials; however, seeks to limit Kim *et al.* by the preferred embodiments such as corn protein extract, hydroxypropylmethylcellulose phthalate, and shellac. *See* p. 7 of Response filed 01/28/2009.

However, as pointed out in *In re Buehler*, 515 F2d 1134; 185 USPQ 781, 786 (CCPA 1975), "the question under 103 is whether the subject matter as a whole would have been obvious, *not* whether the differences would have been obvious." (Emphasis added.) For this reason, one of ordinary skill in the art would recognize that the prior art

cited above identifies compositions comprising water soluble polymers, binding agents such as carrageenan, gellan gum, and lubricants such as glyceryl monostearate that elicit properties such as having a delayed and/or controlled release profile. In other words, the prior art teaches, as a whole, formulations that suggest the usefulness of hydroxypropylmethylcellulose, carrageenan and gellan gum as coating materials.

The Examiner disagrees with Applicant's conclusion, "that the specific combination of coating ingredients in the specified amounts recited by the present claims is much more that a predicable use of known ingredients." First, the components used by Applicant are known in the art, and their useful properties are known in the art. Thus, the selection of one among a group would be an informed selection. Further, the instant claims lack specificity. For instance, Claim 1 calls for 40-95 % of a water soluble polymer having particular properties. As evidence by Claim 2, there are several polymers and "mixtures thereof" which share those properties. Likewise, Kim *et al.* recites on p. 7 that "when coating materials for swelling are used, it is used in the amount ranging from 30 to 95% by weight." In other words, the instant claims are no more specific than those in Kim *et al.*

The Examiner notes that Applicant characterizes Chen *et al.* as a tablet having delayed release properties and such a tablet included glyceryl monostearate. Applicant states that Chen *et al.* fails to teach the specific overcoated shell portion and that the granules should be compressed to form a tablet. In response, the reference was used as evidence that glyceryl monostearate is a commonly used lubricant for delayed release applications. *See* J.C. Carter *Pharmaceutical Canada* 2003, 4(1) and J.C.

Carter *Pharmaceutical Canada* 2001, 2(3) – both references are discussed below with respect to what is commonly known in the art regarding compressed cores and lubricants.

The Examiner disagrees with Applicant distinguishing Sangekar *et al.* from the instant application because the patent is drawn to an immediate release drug formulation. The reference was only used to identify the viscosity of known water soluble polymers because the instant claims define limit the polymers by the properties they share.

For these reasons, and the reasons set out in the rejection below, the 103-obviousness-type prior art rejection is maintained herein.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The scope and contents of the instant claims - Claims 1-8, 17-23, 32-37 are drawn to a pharmaceutical formulation comprising: A) a compressed core having any active ingredient (the list of active ingredients in Claims 1 & 17 essentially include any known drug), in the form of a tablet or capsule; and B) an overcoated shell portion comprising a water-soluble polymer, carrageenan, and gellan gum; wherein said overcoated shell portion elicits properties of a delayed and/or controlled release profile.

The instant claims are not drawn to any specific active ingredient. The examples in the specification utilize ibuprofen as an active ingredient for analyzing the overcoated shell portion. Thus, the crux of the invention is the composition of the overcoated shell portion, which is presumed to be applicable to any of the active ingredients listed.

Claims 36 & 37 are product-by-process claims. "Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985); see MPEP 2113.

Claims 1-8, 17-23, 32, 34, 36, & 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim *et al.* (WO 99/20745; formerly referred to by the Agent "Choi" and not the inventor Kim *et al.*) in view of Chen *et al.* (US 5,922,352) and Sangekar *et al.* (US 4,992,277).

1. Determining the scope and contents of the prior art - Kim *et al.* is directed to an enteric coated granule. The coated granule contains lactic acid bacteria and is coated with a water-miscible coating material (p. 4, first and fourth paragraph). The lactic acid bacteria is prepared by first coating the bacteria-containing seed with a water-miscible coating material and then further coating the first coated product with a second coating (page 4, second paragraph). The water-miscible coating that can be utilized include hydroxypropylmethylcellulose (p. 4, fourth paragraph) and gellan gum (p. 5, first paragraph). The first coating is utilized in an amount of 1 to 80% by weight (p. 5, third paragraph). The second coating material can include one or more coating materials that include hydroxypropylmethylcellulose, carrageenan, and gellan gum (p. 6, second paragraph). The one or more materials are utilized in an amount of 1 to 95% by weight (p. 8, first paragraph). The coating process is carried about by processes known in the art such as utilizing a fluidized bed granulator, CF-granulator, and the like (p. 8, second paragraph).

2. Ascertaining the differences between the prior art and the claims at issue – Kim *et al.* does not specify that the coating is made of hydroxypropylmethylcellulose, carrageenan, and gellan gum; that the core is compressed; or the specific use of glycerol monostearate. However, these deficiencies are addressed by Chen *et al.*

Chen *et al.* is directed to enteric coated calcium channel blocker compounds. The granules which form the compressed core contain additionally known excipients such as a tablet lubricant such as glyceryl monostearate (col. 3, ll. 4-17). This core is

then coated with pharmaceutically acceptable polymers such as hydroxypropylmethyl cellulose (col. 3, ll. 1-3).

Further, Kim *et al.* does not specify the viscosity of hydroxypropylmethylcellulose or that the formulation exhibits a burst release formulation. However, these deficiencies are cured by Sangekar *et al.*

Sangekar *et al.* is directed to an immediate release formulation. The core comprises diltiazem and is coated with a swellable hydrophilic polymer (abstract and col. 2, ll. 62-65). The hydrophilic polymers utilized include hydroxypropyl methylcellulose which can be used alone or in combination with other hydrocolloids such as guar gum (col. 3, ll. 1-7). The hydroxypropyl methylcellulose is commercially available in various grades under several trade names including METHOCEL E, METHOCEL F, and METHOCEL K. These commercially available products have viscosities in a 2% aqueous solution ranging from 3500 to 100,000 cps (mPas) (col. 3, ll. 16-43).

3. Resolving the level of ordinary skill in the pertinent art – the level of ordinary skill in the art may be found by inquiring into: (1) the type of problems encountered in the art; (2) prior art solutions to those problems; (3) the rapidity with which innovations are made; (4) the sophistication of the technology; and (5) the education level of active workers in the field. *Custom Accessories, Inc.*, 807 F.2d at 962. All of those factors may not be present in every case, and one or more of them may predominate. *Envtl. Designs, Ltd. v. Union Oil Co.*, 713 F.2d 693, 696 (Fed.Cir.1983).

Based on the typical education level of active workers in the field of biology, chemistry, biochemistry, pharmacology, etc., as well as the high degree of sophistication required to solve problems encountered in the art, the Examiner finds that a person of ordinary skill in the art would have at least a college degree in one of disciplines common in the field and at least four years of work experience, i.e. a masters or doctorate level scientist.

With respect to the formulation art, the following references highlight some of the knowledge that a person of ordinary skill in the art would have. The reference by J.C. Carter *Pharmaceutical Canada* 2003, 4(1) teaches that there are three general processes for producing tablets and capsules: direct mix, dry granulation, and wet granulation (p. 2). Each of the processes involves compressing the drug substance (granules) with excipients. Further, a tablet or capsule form will generally contain the following components: active ingredient, binder, solvent, fillers/diluents, disintegrating agents, glidant, anti-adherent, lubricant, etc. (pp. 2-5).

Lubricants are one class of functional excipients that are considered essential to most solid oral dosage forms. While the "ideal" lubricant for use in all occasions does not exist, the selection of a lubricant for manufacturing is routine in the art. J.C. Carter *Pharmaceutical Canada* 2001, 2(3).

Calcium salts are another classic excipient commonly used in the formulation art as a filler. R.H. Dave, *Drug Topics: Overview of pharmaceutical excipients used in tablets and capsules*, 10/28/2008, downloaded from the internet 06/09/2009. The reference includes a table of excipients used in the art covering about 200 drugs; and

the column on the right cites the common uses for each excipient. For example, glyceryl monostearate is used as tablet and capsule lubricant. Hydroxyl propyl methyl cellulose (HPMC) is uses as a rate-controlling polymer and a viscosity-increasing agent. *See, i.e.,* Yamamoto *et al.* (US 5,756,123), which is directed to a capsule comprising hydroxypropyl methylcellulose, carrageenan and potassium and/or calcium ions (*See* abstract). It is disclosed that carrageenan is a gelling agent and that the potassium ion is a co-gelling agent. It is disclosed that the shapability of the hydroxypropyl methyl cellulose is improved by blending carrageenan as a gelling and gelling this carrageenan with a co-gelling agent (col. 2, ll. 43-53).

A person having ordinary skill in the art would be of high skill, and would know or have the means to know which formulation components to select based on known properties (i.e. HPMC is a viscosity-increasing agent). It was held that a person having ordinary skill in the art has good reason to pursue known options within his or her technical grasp *KSR International Co. v. Teleflex Inc.* 82 USPQ 2d 1385 (2007). Thus, the prior art need not explicitly provide a suggestion to combine known elements. In this case, one of ordinary skill in the art would be able to select the common components based on the desired properties in routine optimization studies for a particular active ingredient.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness – the instant application combines a high molecular weight, water soluble polymer with carrageenan, and optionally gellan gum and/or a lubricant such that the composition can be dispersed in water and the viscosity of the

dispersion is manageable due to the presence of the carrageenan. *See* specification pp. 2-3. For this reason, it appears that the advantage of the instant application over the prior art may pertains to an easier method for molding cores containing an active ingredient with the polymer compositions. However, there is no evidence of a long-felt need or that there is a commonly recognized problem in the art for which the instant compositions solve. In other words, these secondary considerations have been considered but are not dispositive of non-obviousness.

Conclusion – the formulation composition as instantly claimed is drawn to a combination of known ingredients in the art. As such, the known ingredients have known properties; and one of ordinary skill in the art would have predictable expectations as to how those properties will contribute to the composition when combined with other ingredients. The claims, drawn to of a formulation composition, have been herein shown to be *prima facie* obvious and the specification fails to produce evidence of unexpected results, a long-felt industrial need, or other secondary considerations to overcome the lack of novel combination known ingredients. As such, one skilled in the art would thus be motivated to optimize the teachings by Kim *et al.* with the teachings of Chen *et al.* and Sangekar *et al.* in order to arrive at the instant composition with an expectation of success (delayed release of active ingredient).

Claim Objections

Claims 33 & 35 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Specifically, Claims 33 & 35 depends from Claim 32, depends from Claim 1. Claim 32 is drawn to "said predetermined time." Thus, neither Claim 1 nor 32 address the "pH of the media," and for this reason, Claims 33 & 35 fail to further limit the subject matter of a previous claim. The Examiner suggests cancelling the claims.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jason M. Nolan whose telephone number is (571) 272-4356 and e-mail is Jason.Nolan@uspto.gov. The examiner can normally be reached on Mon - Fri (9:00 - 5:30PM). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph M^{c}Kane can be reached on (571) 272-0699. The USPTO fax number for applications is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system, (either Private PAIR or Public PAIR). Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. For questions on Private PAIR system, contact the Electronic Business Center at (866) 217-9197.

/Jason M. Nolan/

Examiner, Art Unit 1626

/Kamal A Saeed/

Primary Examiner, Art Unit 1626